<Bioinformatics Center> Bioinfonnatics Training Unit

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Scope of Research

Evolutionary studies based on molecular biology is called "molecular evolutionary biology", which is one of the origins of the current bioinformatics. Living organisms have acquired wide variety of functions during the course of the evolution by changing the information encoded by the genomes. Inversely, reconstruction of the evolutionary history related to the functions would bring us a great insight into the acquired functions and the life. Furthermore, such evolutionary information is useful for practical fields such as drug design and proteins engineering. We develop new methodologies with evolutionary information, to extract biological knowledge from various molecular biological data including sequence and structure data of individual genes and proteins, genome data, and expression profile data. We also analyze the data of molecular biology from the evolutionary viewpoint, to obtain novel biological knowledge.

Research Activities (Year 2002)

Presentations

Pharmacoinformatics & Drug Design, Hiroyuki Toh, Symposium Roundtable: Science of Drug Design: Now and Future, The 122th Annual Meeting of the Pharmaceutical Society of Japan, Chiba, 27, March.

Three novel repetitive units of Reelin, Hisako Ichihara, Hisato Jingami, and Hiroyuki Toh, The 55th annual meeting of the Japan Society for Cell Biology, Yokohama, 21 May.

Moleular Phylogenetic Analysis of PCNA and the homologues. Hiroyuki Toh, Kazuya Osaka, and Yoshizumi Ishino, The 2nd Annual Meeting of the Protein Science Society of Japan, Nagoya, 13, June.

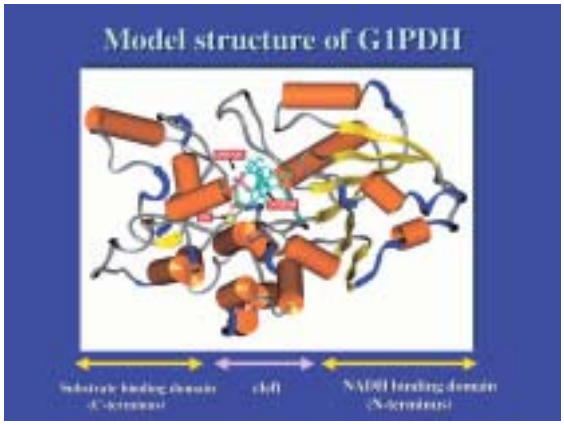
Inference of Genetic network from Expression Profile Data, Toh, H., and Horimoto, K., Workshop Bioinformatics orienting the analysis of inter-molecular interaction, The 2nd Annual Meeting of the Protein Science Society of Japan, Nagoya, 15, June.

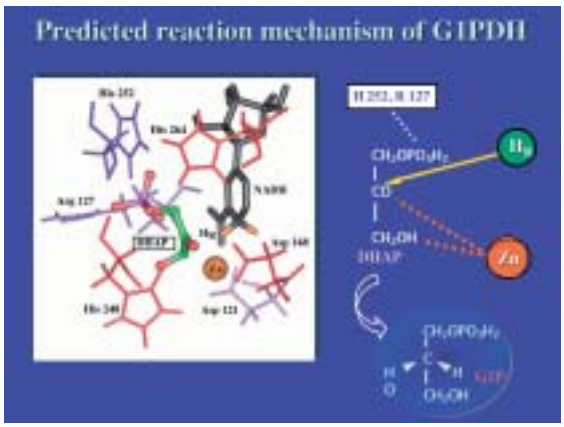
Three novel repetitive units of Reelin, Hisako Ichihara, Hisato Jingami, and Hiroyuki Toh,The 3rd annual meeting of Chemo-Bio Informatics Society, Tokyo, 19, September.

The analysis of membrane stereochemistry with the homology modeling of sn-Glycerol-1-phosphate dehysrogenase, Hiromi Daiyasu, Hiroyuki Toh, Takaaki Hiroike, Yousuke Koga, The 3rd annual meeting of Chemo-Bio Informatics Society, Tokyo, 19, September.

An Analysis of Membrane Stereochemistry with Homology Modeling of sn-Glycerol-1-Phosphate Dehydrogenase

Different enantiomeric isomers, sn-glycerol-1-phosphate and sn-glycerol-3-phosphate, are used as the glycerophosphate backbones of phospholipids in the cellular membranes of Archaea and the remaining two kingdoms, respectively. In Archaea, sn-glycerol-1-phosphate dehydrogenase is involved in the generation of sn-glycerol-1-phosphate, while sn-glycerol-3-phosphate dehydrogenase synthesizes the enantiomer in Eukarya and Bacteria. The coordinates of sn-glycerol-3-phosphate dehydrogenase are available, al-





though neither the tertiary structure nor the reaction mechanism of sn-glycerol-1-phosphate dehydrogenase is known. Database searching revealed that the archaeal enzyme shows sequence similarity to glycerol dehydrogenase, dehydroquinate synthase, and alcohol dehydrogenase IV. The glycerol dehydrogenase, with coordinates that are available today, is closely related to the archaeal enzyme. Using the structure of glycerol dehydrogenase as the template, we built a model structure of the Methanothermobacter thermautotrophicus sn-glycerol-1-phosphate dehydrogenase, which could explain the chirality of the product. Based on the model structure, we have determined the following: (1) The enzyme requires a Zn^{2+} ion for its activity. (2) The enzyme selectively uses the pro-R hydrogen of the NAD(P)H. (3) The putative active site and the reaction mechanism were predicted. (4) The archaeal enzyme does not share its evolutionary origin with sn-glycerol-3-phosphate dehydrogenase.

Ammonium-assimilating enzymes: physiological and phylogenic perspectives

Nitrogen-assimilating enzymes are important to produce organic nitrogen compounds. In the nitrogen-assimilating process, ammonium is converted into glutamate. There are two alternative pathways for the ammonium assimilation. One of them is composed of glutamate dehydrogenase (GDH), while the other consists of glutamine synthetase (GS) and glutamate synthase (GOGAT). Both pathways seem to be essential because our research clarified that many organisms had both pathways. The phylogenetic analyses of the three enzymes, GDH, GS, and GOGAT revealed that each enzyme had two or three paralogous subtypes. In many cases, however, each organism utilizes only one copy of subtypes. The adoption of the subtypes does not reflect the phylogenetic relationship.

Inokuchi R, Kuma K, Miyata T, and Okada M, Physiologia Plantarum, 116, 1-11, (2002).